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Review article

Nature Nano-Worriers: Phytoconstituents Loaded Lipid Nano Particles against Cancer

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ABSTRACT

This review explores the potential of nanotechnology and phytomedicine in the fight against cancer. It explores the challenges posed by cancer treatment and the potential of using lipid nanoparticles for drug delivery. This article discusses the advantages of using phytochemicals as anti-inflammatory drugs and highlights the role of nanocarriers in improving their bioavailability and therapeutic effects. Different types of lipid-based nanoparticles, such as liposomes, solid lipid nanoparticles, and nanostructured lipid carriers, have been studied for their ability to trigger a response in cancer cells. This review also discusses the challenges and future directions in the field and highlights the need for further research and development to exploit the full potential of lipid nanoparticles loaded with botanical ingredients in cancer therapy.

Keywords: Nanotechnology, Nanomaterials, Lipid-based nanoparticles, Liposome, Solid lipid nanoparticles, Nanostructured lipid carriers, Niosome, Phytoconstituents, Phytomedicine.

INTRODUCTION

Nano Approaches to Cancer Treatment

Cancer, characterized by abnormal cell growth, is a major global health problem affecting all ages and populations. Its far-reaching consequences require increased awareness, reliable prevention, and accessible health services. The fight against cancer requires an integrated approach from governments, health professionals, researchers, and support groups. Innovations in treatment, early detection, and supportive care are essential, along with education and policy efforts to reduce morbidity and improve outcomes. By focusing on prevention and comprehensive care, society can better manage the far-reaching impacts that cancer has on individuals and communities around the world [1].

Cancer characterized by its diverse transformations and complexity, is a major challenge in medical understanding and treatment. Over the years, dedicated researchers have made significant efforts to develop innovative therapies to combat cancer. Despite remarkable progress and improved survival rates, many obstacles remain in developing and implementing precise and safe interventions. The goal is to use techniques such as chemotherapy, radiotherapy, hyperthermia, and various other treatments to effectively target cancer cells directly while minimizing unintended side effects. Precision medicine aims to improve cancer treatment by customizing it for each patient based on their genetic makeup and other factors, leading to more effective and personalized care. There are also ongoing research efforts to improve our understanding of tumor biology, improve early detection methods, and improve the overall effectiveness of existing therapies. As the medical community continues to work together in this challenging

situation, the ultimate goal is to improve treatments that maximize patient benefit, optimize outcomes, and minimize side effects [2].

Cancer is a global health crisis affecting over 100 countries, straining healthcare systems and impacting lives across all socio-economic levels. As cancer threatens to become the leading cause of death, urgent action is needed in research, prevention, and treatment. To improve global health and life expectancy, we must unite to combat this pervasive disease and strive towards a future where its impact is significantly reduced [3].

Cancer is the number one cause of death worldwide, and breast cancer is one of the most common types affecting women. The risk increases with age and is influenced by genetic and environmental factors. In 2020, an estimated 2.3 million women were diagnosed with breast cancer, and 685,000 died from the disease. The disease is challenging for healthcare systems and families due to its high morbidity and emotional impact. Advances in screening, early detection, and treatment are critical to improving survival rates and quality of life. Continued research, awareness, and improved access to treatment are essential to eradicate breast cancer and reduce its global impact [4].

By 2040, breast cancer cases are expected to increase by 40% to more than 3 million cases per year, and deaths are expected to increase by 50% to more than 1 million. These projections highlight the urgent need for improved prevention, early detection, and treatment. To address this crisis, global health systems must raise awareness, invest in advanced technologies, promote collaboration to reduce the impact of breast cancer, and work toward a future where no one loses a life due to the disease [5].

A woman is diagnosed with breast cancer every 14 seconds, highlighting the urgent need for advanced treatments. Phyto-medicine and nanotechnology are emerging as promising solutions, offering more targeted and personalized approaches. Combining traditional herbal medicine with modern nanomedicine, these innovations aim to revolutionize treatment, improve patient outcomes, and reduce the global burden of breast cancer. This progress reflects a strong commitment to enhancing cancer care and developing effective, personalized treatment options [6].

Cancer nanotechnology, a method of delivering anticancer drugs, has been developed as a promising cancer treatment. Nanoparticles with sizes ranging from 1 to 1000 nanometers enhance drug delivery by improving solubility and stability. In cancer treatment, they can target tumors more precisely, reduce side effects, and release drugs in response to specific stimuli. Nanoparticles functionalized with targeting ligands increase selectivity and efficiency while minimizing off-target effects. Among various nano formulas in oncology, lipid-based formulations stand out due to significant recent advancements in their preparation and innovative alternatives [7].

Lipid-based nanoparticles (LBNPs), like liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs),

Have gained much interest in drug development and cancer treatment because of their various helpful functions. These nanoparticles excel in encapsulating hydrophobic and hydrophilic drugs, enhancing their stability and bioavailability. They are known to be biocompatible and have low toxicity, making them suitable for long-term treatment. Also, their long-lasting effects allow for steady and controlled drug release, which helps improve the treatment's effectiveness and duration while reducing side effects. Combining these properties positions LBNPs as a powerful tool for advancing targeted and effective therapies [8].

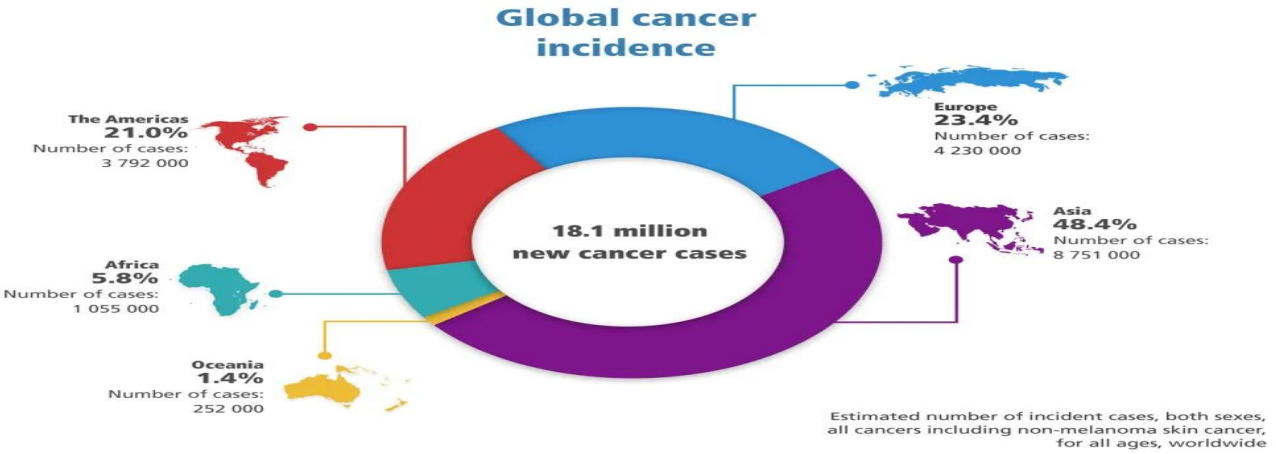
Lipid nanosystems may include chemical modifications to evade detection. They may enhance the immune system (gangliosides or polyethylene glycol (PEG)) or improve drug solubility. They may also be formulated as pH-sensitive agents to promote drug release in acidic environments, and they may be linked to antibodies that recognize tumor cells. Or their receptors (e.g., folate (FoA)). Nanomedicine may also be used with other therapeutic strategies to improve patient responses.

Many anticancer drugs such as cisplatin, irinotecan (IRI), paclitaxel (PTX), doxorubicin (DOX) Oxaliplatin, daunorubicin, cytarabine or vincristine have been studied as Nano formulations and some of them have been analyzed in clinical trials or are commercially available for clinical use in: patients. Doxil®, a liposomal formulation encapsulating DOX, was one of the first anticancer drugs. Pharmaceutical Nano systems are used commercially. This review highlights the major contributions of LBNPs that have developed in

recent years. Applications in cancer therapy, including baseline screening of patients [9].

The emergence of nanomedicine delivery platforms represents a significant change in perspectives on integrating new encapsulation methods, phytochemicals, and nanotechnology. The originality of this study lies in exploring the current developments in nanomedicine delivery systems to simultaneously deliver phytochemicals and chemotherapy drugs, with the overall goal of achieving effective cancer control. This text details the rigorous process of selecting phytochemicals for their anticancer properties, analyzes nanocarrier design principles, and investigates the impact of physicochemical factors on drug release kinetics. Drug release kinetics is an important aspect of drug delivery and is influenced by various factors such as solubility, hydrophilicity, ionization state, particle size, and polymorphism. Highly water-soluble drugs are released more rapidly than poorly soluble drugs, while hydrophilic drugs are released more quickly in aqueous environments such as the stomach. The charge of the drug molecule also affects its interaction with the delivery system, affecting release. The smaller the drug particle, the greater the surface area, which allows more drugs to be released, resulting in a faster release rate. Different crystal forms of the drug may also have different solubilities, and the solubility rate affects the release. Understanding these factors allows scientists to develop drug delivery systems to control the release profile and achieve the desired therapeutic effect. For example, sustained-release formulations of hydrophobic drugs: ensure slow, uniform release over time. Furthermore, this discussion covers the following nanoformulation studies: Combining synthetic and herbal ingredients, focusing on improving herbs and oils—oncology treatment. The revolutionary ability of this association lies not only in the novel combination of elements but also in its comprehensive methodology of redefining treatment; it offers a reliable alternative to overcome the current barriers in oncology [10].

Figure 1: Worldwide cancer percentage Exploring Nanodrug Deliver: Types, Features, And Therapeutic Potentia

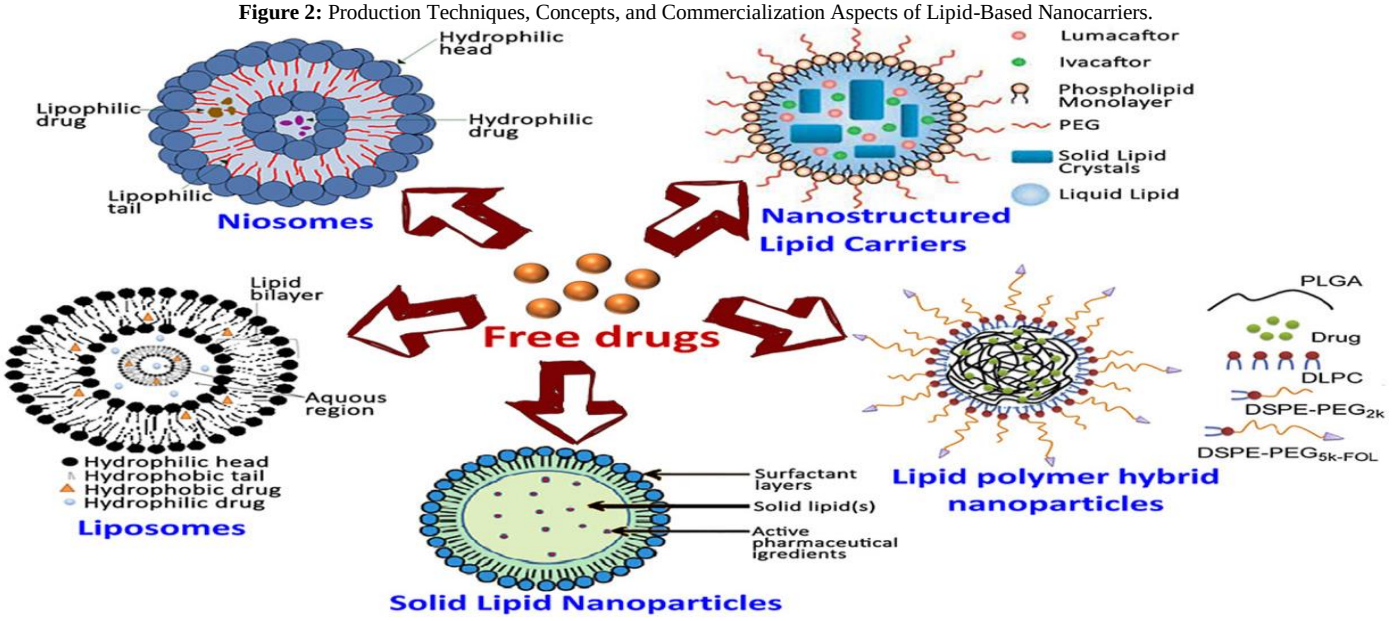


Worldwide Cancer Trends and Challenges: -

Cancer is the leading cause of death globally, responsible for 10 million deaths in 2020. It is one of the deadliest diseases, and its death rates continue to rise. In 2020, the most common cancers were breast (2.26 million cases), lung (2.21 million), prostate (1.41 million), skin (1.2 million), and colon (1.93 million). In India, cancer cases were projected to increase from 14.6 million in 2022 to 15.7 million by 2025. In 2023 alone, India saw 1.96 million new cases and 609,820 deaths. Effective cancer prevention and treatment rely on current data, including surgery, radiotherapy, and systemic therapies like chemotherapy and targeted biological treatments [11]. Anticancer drugs are designed to fight cancer cells and are widely distributed throughout the body, posing a risk to healthy cells as well. For this reason, achieving targeted drug delivery to specific sites is important, requiring the development of delivery systems that are much smaller than the intended target. Using the power of nanotechnology, drugs can be precisely targeted to the intended site of action, revolutionizing personalized medicine. This breakthrough in drug delivery not only improves the therapeutic efficacy of drugs but also reduces harmful effects on non-target tissues. Traditional approaches to treating solid tumors typically involve a combination of surgical removal, radiation therapy, and chemotherapy. Although these treatments are effective in treating cancer, they are associated with many side effects that can seriously impact a patient's quality of life, highlighting the urgent need

for more targeted and less toxic treatment options in oncology [12].

Figure 2: Production Techniques, Concepts, and Commercialization Aspects of Lipid-Based Nanocarriers.



Liposomes

In 1968, Bangham and his colleagues made a landmark discovery in lipid science by demonstrating that lipids have the remarkable ability to form bilayer structures when placed in an aqueous environment. This important discovery led Sessa and Weissman to coin the term "liposome" in the same year. Liposomes have a water-filled center surrounded by a layer of phospholipids. The fatty chains are on the inside, while the water-loving heads face outward, toward the surrounding water. This unique structure makes liposomes invaluable for encapsulating and delivering therapeutics to specific sites in the body. The range of phospholipid components that can be used in liposome formulations is extensive, including both natural sources such as phosphatidylcholine from eggs or soybeans, and synthetic alternatives such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), and phosphatidylserine (PS). Among them, 2-distearoyl-sn-glycero-3-phosphocholine (DSPC) is one of the most widely used PC forms in liposome formulations due to its stability and compatibility with drug delivery systems [13, 14].

The biocompatibility and biodegradability of liposomes make them a highly studied delivery system. The main component of these nanoparticles, phospholipids, are amphiphilic, meaning they are structured in a bilayer structure. Liposomes can form vesicles in water, which increases the stability and solubility of the anticancer drugs they contain. They can contain hydrophilic or hydrophobic drugs. In addition to phospholipids, other substances such as cholesterol can be added to liposomes. The stability of these nanoparticles in the bloodstream is improved because cholesterol reduces particle fluidity and increases the permeability of hydrophobic drugs through the bilayer membrane. Cholesterol-modified liposomes can have various bilayer structures: multilamellar vesicles (MLVs): have multiple bilayers and range in size from 0.5 nm to 10 nm; large unilamellar vesicles (LUVs): are larger than 100 nm and have a single bilayer; and small unilamellar vesicles (SUVs): have an intermediate size of 10–100 nm [15].

Liposomal drug delivery offers several advantages over conventional therapies, including minimizing systemic side effects of encapsulated drugs, better control of pharmacokinetics, predictable drug release patterns, and passive and active tumor targeting. Encapsulation of drugs into liposomes can be achieved in two ways: passive and active approaches. In passive loading, the drug is incorporated during liposome formation, a process that is influenced by the chemical properties of the drug, such as hydrophilicity or hydrophobicity. For example, hydrophilic drugs can be combined with a hydration buffer during liposome preparation, while hydrophobic drugs can be incorporated with phospholipids during lipid membrane insertion and lipid membrane formation. However, passive methods often result in lower encapsulation efficiency of hydrophilic drugs due to limited interaction with the lipid membrane. This effect can be increased by attaching hydrophobic chains to the drug molecule, which promotes its incorporation into the lipid bila [16].

The distribution of passive target drugs in the body after intravenous administration depends on the size of the microparticles. Smaller-sized nanoparticles generally exhibit higher tissue permeability and reduced renal excretion [17].

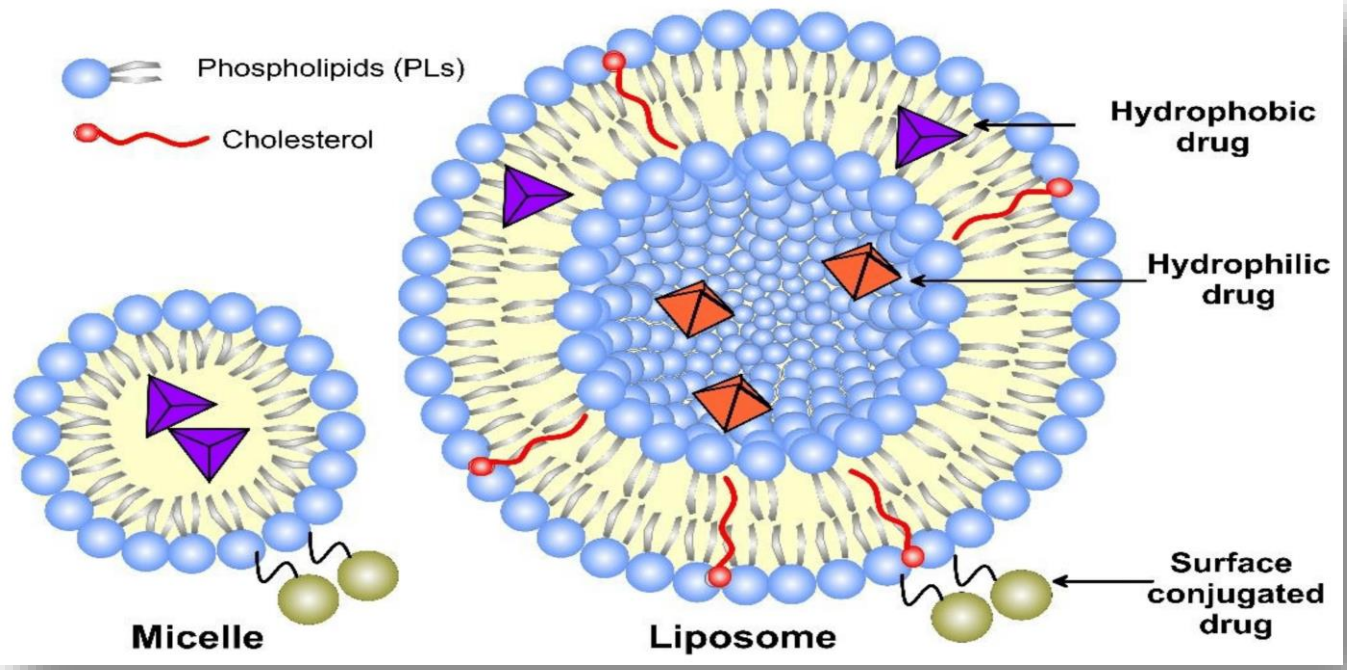
In 2016, Jiang et al. successfully developed a nano lipid carrier (ETP-CUR-NLC) containing both ETP and CUR. This innovative formulation demonstrated remarkable therapeutic profiles in vivo, with minimal cytotoxicity to normal tissues and significantly enhanced cytotoxicity to tumor tissues [18].

They co-encapsulated Res and PTX into PEGylated liposomes, which demonstrated potent cytotoxic effects against drug-resistant MCF-7/ADR tumor cells in vitro. Furthermore, the formulation improved drug bioavailability and enhanced tumor retention in vivo [19].

Active targeting can be achieved by modifying liposomes with specific ligands. For example, the surface of liposomes can be modified with HA (hyaluronic acid), which enhances the specific adhesion of cancer cells to the HA ligand. This modification increases the activity and permeability of the liposomes, which increases drug efficacy, reduces side effects, and provides the ability to overcome drug resistance at standard doses. Surface functionalization of cationic liposomes and HA-modified targeting NLCs was used for co-delivery of CBX and silibinin (SIL) using ethanol injection for GEM and BCL precursors via nanoprecipitation technique. In vivo, antitumor studies showed that HA-GEM-BCL NLCs demonstrated the most potent antitumor effects against pancreatic cancer in animal models with reduced systemic toxicity compared to other liposomes. Moreover, in vitro experiments showed that the cellular uptake efficiency of HA-GEM-BCL by NLCs was significantly higher than that of other NLC formulations [20].

They developed pH-sensitive liposomes coated with chitosan, a glycol derivative with amino-terminal groups. These groups impart a negative surface charge, allowing the liposomes to interact with the acidic extracellular environment of positively charged tumors. DOX was encapsulated inside the liposomes, which significantly enhanced their anticancer efficacy. PH-responsive nanostructured lipid carriers loaded with DOX and β-ELE (DOX/ELE Hyd NLC) were developed for lung cancer treatment. In acidic tumor sites, the acid-sensitive hydrazone bond of NLCs was cleaved to promote drug release. Compared with pH-sensitive NLCs and single-drug loaded NLCs, pH-sensitive and dual-drug loaded NLCs showed significantly higher cytotoxicity and tumor inhibition rates [21].

Figure 3: Visualizing Micelle and Unilamellar Liposome Architectures: Exploring Drug Placement



Solid lipid nanoparticles

Solid lipid nanoparticles (SLNs) with sizes ranging from 1 to 1000 nm are considered advanced colloidal nanocarriers for drug delivery. These nanoparticles encapsulate hydrophilic and hydrophobic drugs, combining the beneficial aspects of polymeric microparticles and

liposomes. Physiological lipids can be dispersed in aqueous surfactant solutions to form submicron colloidal systems known as "solid lipid nanoparticles" (SLNs), which remain stable in the body despite their small size. Recently, SLNs have attracted attention as promising nano-delivery systems for cancer therapy. Their advantages over traditional colloidal carriers include enhanced cellular uptake, smaller size, larger surface area, higher drug loading, sustained and targeted drug release, improved bioavailability with reduced toxicity, and fewer side effects [22].

SLNs are formulated as submicron lipid emulsions in which the liquid lipids (oils) are replaced by solid lipids. They consist of solid lipids, emulsifiers, and water or a solvent. Lipids commonly used in these formulations include triglycerides (e.g., tristearin), partial glycerides (fatty acid esters of glycerol), fatty acids (e.g., stearic acid and palmitic acid), steroids (e.g., cholesterol), and waxes (e.g., cetyl palmitate). They act as a matrix material for encapsulating the drug. Stabilizers such as Pluronic F68 and Pluronic F127 are used to maintain the stability of the lipid dispersion.

The preparation of SLNs often begins with a dispersed system as a precursor or template, or through specialized methods such as spray drying, spray curing, and electrospray. Most precursors used in SLN formulations are emulsions. Solid lipids, which are solid at room temperature, are heated above their melting point to form liquid lipids, which are then emulsified with an aqueous solution. The droplets eventually solidify into SLNs. Common methods for preparing SLNs include hot or cold high-pressure homogenization, microemulsion methods, and precipitation of lipid particles by solvent evaporation.

Homogenization methods use extreme temperatures (hot or cold) and high pressures of 100–200 bar as the lipids pass through narrow micrometer spaces. Under these conditions, shear stress produces small particles. The microemulsion method includes low-melting point lipids, emulsifiers, co-emulsifiers, and water. During mixing, the hot microemulsion is dispersed in cold water (2°C to 3°C) at a microemulsion-to-water volume ratio of 1:25 to 1:50. The lipid phase is then precipitated to form smaller particles, and the excess water and emulsifier are removed through ultrafiltration.

The emulsification-solvent evaporation method is a method in which hydrophobic components are dissolved in an organic solvent and then emulsified in water using a homogenizer to achieve uniform particle size reduction. The organic solvent is then evaporated using a stirrer or rotary evaporator to form SLN. This method is particularly advantageous for mixing heat-labile drugs, as it avoids heat stress. Other methods for preparing SLN include emulsification-solvent diffusion, sonication, melt dispersion (hot melt capture), double emulsification, and spray drying [23].

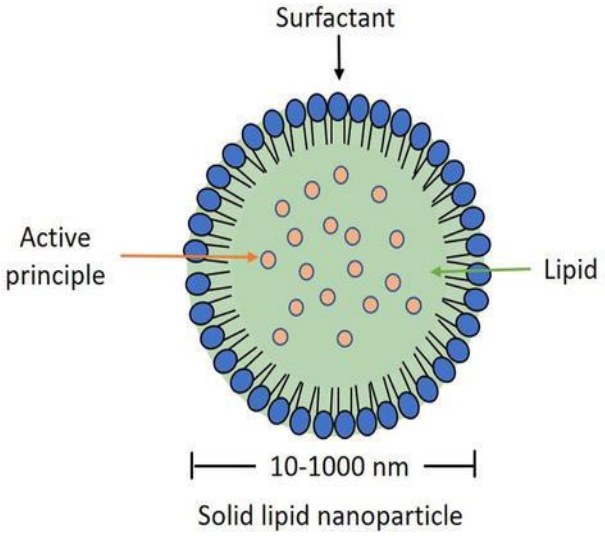
The rapidly developing field of nanotechnology includes SLNs, which hold great promise for clinical treatment, drug delivery, research, and related scientific fields. Due to their unique size-dependent properties, lipid nanoparticles offer opportunities for the development of innovative therapeutics. SLNs are currently used in a wide range of medical and cosmetic applications, including the treatment of infections, cancer, diabetes, cardiovascular diseases, neurological disorders, and cosmetic formulations. In a pharmaceutical context, the most effective carriers for drug delivery are nanomaterials that are both biodegradable and biocompatible. Examples of advanced drug delivery technologies that provide sustained and controlled release include polymeric microspheres, liposomes, nanoparticles, hydrogels, transdermal and buccal systems, and implants [24].

This article will be useful for researchers studying the use of phytochemicals in SLNs for cancer therapy. Phytochemicals have been successfully used for many years to treat various types of cancer. Figure 1 shows phytochemicals loaded into SLNs and delivered to target cancer cells. Lipid carriers have been widely studied to carry active ingredients of synthetic drugs for a wide range of cancer therapies, especially those that are difficult to treat with conventional therapies. Numerous research groups have used SLNs to effectively deliver phytochemicals to enhance their anticancer effects [25].

Over the past 30–40 years, researchers from academia and industry have increasingly focused on lipid nanocarriers for the delivery of bioactive compounds. Traditional drug delivery and administration methods are fraught with numerous problems, including poor patient compliance, rapid metabolism, low bioavailability, dose inconsistency, unpleasant side effects, and drug toxicity. However, nanocarrier systems, such as liposomes, billosomes, niosomes, solid lipid nanoparticles (SLNs),

ethosomes, ribosomes, and polymeric nanoparticles, have been developed to overcome these limitations and provide solutions for targeted delivery. Lipid nanoparticles have been shown to significantly enhance absorption and bioavailability while reducing side effects, highlighting their potential as promising therapeutic drug delivery vehicles. Among them, solid lipid nanoparticles (SLNs) have emerged as an excellent nano-delivery system widely used for the controlled oral release of plant compounds for the treatment of various chronic diseases [26].

Figure 4: General structure of solid lipid nanoparticles



Nanostructured Lipidic Carriers

Nanostructured lipid carriers (NLCs) have been specifically designed to overcome the limitations of solid lipid nanoparticles (SLNs) by improving drug delivery and enhancing the stability of encapsulated drugs. In NLCs, drugs are placed in a mixture of solid, liquid, and lipid phases, allowing for changes in composition. This feature distinguishes NLCs from SLNs because the NLC matrix intentionally becomes less crystalline or even amorphous during solidification, unlike the rigid crystalline core of SLNs. Although the configuration of NLCs is similar to SLNs, the key difference lies in the matrix structure. SLNs generally dissolve drugs in lipids, while NLCs dissolve or solubilize drugs into liquids and lipids dispersed in an aqueous medium containing emulsifier. During homogenization and storage, SLNs tend to crystallize into solids, limiting drug retention and potentially leading to drug leakage or reduced drug availability. In contrast, NLC combines solids and liquid lipids to form an amorphous matrix, which can not only accommodate many drugs but also prevent drug leakage, thereby improving the stability and overall efficiency of the drug. NLCs can be classified into three types: Type I, featuring a disordered and imperfect matrix; Type II, containing oily Nano compartments; and Type III, characterized by a solid, non-crystalline amorphous matrix [27].

The researchers compared solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) and found that NLC was superior to SLN in key areas such as drug release mechanism, stability, drug encapsulation efficiency, and nasal tissue absorption. These results highlight the significant benefits of NLC in providing controlled and sustained drug release, maintaining drug stability, improving drug encapsulation, and improving tissue energy absorption. This study demonstrates the potential of NLCs as an ideal strategy for drug delivery, which has important implications for future research in the development of more effective drugs [28].

Many technologies can be used for NLC, such as phase inversion, film contract technology, hot melt extrusion (HME) technology, high-pressure homogenization (HPH), heavy emulsion evaporation, heavy emulsion diffusion, heavy injection, microemulsion, Double emulsion technology, ultrasonic or high-speed homogenization, phase inversion, and film shrinkage technology. Recent studies have highlighted the increasing role of nanostructured lipid carrier (NLC) formulations in various clinical applications. This new technique is of particular interest for the delivery of harmful drugs. Their popularity stems from their biocompatibility and lipid-based structure that enhances the solubility of drugs that are usually difficult to dissolve. NLCs provide a safe and effective platform for drug delivery, enhanced bioavailability, and therapeutic efficacy. Their ability to encapsulate and protect chemical molecules adds to their appeal. As nanotechnology and lipid science continue to advance, NLCs are expected to revolutionize drug delivery, benefiting patients and global health [29].

Many researchers have developed nanostructured lipid carriers (NLCs) for the treatment of various cancers, including lung, brain, and breast cancer. Specifically, Wang et al. developed NLCs loaded with two chemotherapy drugs, paclitaxel and doxorubicin (DOX). Their research demonstrated synergy between these drugs in cancer models, reducing toxicity. Additionally, the dually loaded NLCs demonstrated in vitro activity against NCL-H460 cancer cells, suggesting their potential to improve clinical outcomes while minimizing side effects for human patients [30].

In another study, Ong et al. developed nanostructured lipid carriers (NLCs) loaded with thymoquinone, a compound known for its anticancer properties. These NLCs were administered orally to mice with 4T1 metastatic breast cancer. The results of the study showed that the anticancer effect of thymoquinone in NLC formulations was better than that of thymoquinone alone. In addition, the survival rate was increased in mice treated with thymoquinone-loaded NLC, indicating the ability of NLC to enhance performance in treatment and prolong survival [31].

Researchers also developed nanostructured lipid carriers (NLCs) loaded with both vitamin D and doxorubicin (DOX) and found that simultaneous administration of vitamin D and DOX using the NLC system improved the treatment of MCF-7 breast cancer. Another study found that NLC preparations containing curcumin were effective in the treatment of breast cancer. They found that the immune response was enhanced, particularly in A172 glioblastoma cells. Additionally, in vivo studies using curcumin-NLC in the A172 xenograft mouse model resulted in better therapeutic efficacy at lower doses, suggesting that NLC has the potential to improve drug delivery while reducing the dose [42]. Several research groups have investigated the incorporation of phytochemicals into nanostructured lipid carriers (NLCs) for cancer treatment. For example, Gadag et al. developed NLCs containing resveratrol, a natural product with anti-inflammatory properties, and delivered them to breast tissue using microneedle arrays. This new delivery method increases drug permeability in the body, allowing for better absorption and distribution in tissues. Furthermore, resveratrol-loaded NLCs exhibited in vitro antitumor activity against MDA-MB-231 breast cancer cells, a high-risk cancer type. These findings suggest that the combination of phytochemicals with NLC delivery may enhance the therapeutic potential of natural products in cancer treatment [32].

Niosomes

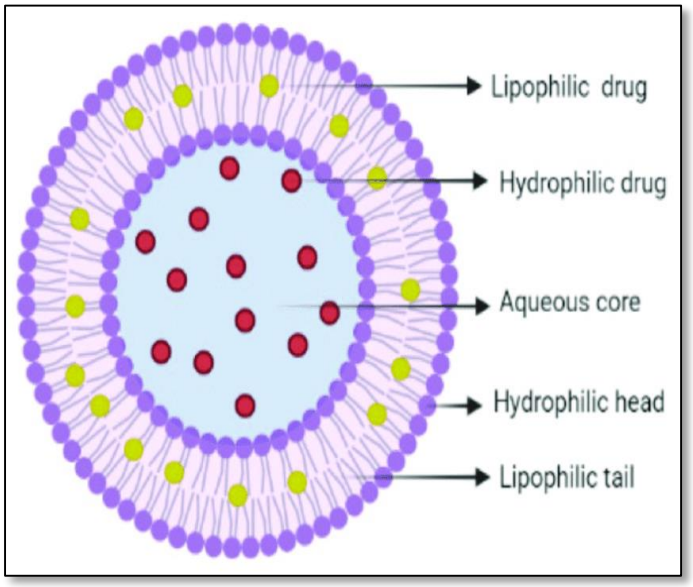
Nanobodies are a novel drug delivery system consisting of nanosheet-like vesicles formed by combining non-ionic surfactants and cholesterol-like lipids. When surfactants are subjected to force (physical mixing and heat), they form stable bilayer vesicles in a hydrophilic environment. In this bilayer structure, the hydrophilic head is always in contact with the surrounding water, while the hydrophobic tail is away from the water. The use of biocompatible, biodegradable, and non-immunogenic surfactants is essential for the production of nanobodies. Liposomes function similarly to liposomes, both in vivo and in vitro, prolonging the circulation time of encapsulated phytochemicals, modifying their texture, and increasing their bioavailability. Nanobodies are designed to increase the solubility and stability of phytochemicals and to provide controlled and targeted release.

Barani et al. Two different niosome formulations were developed. One contains thymoquinone (TQ), a phytochemical extracted from *Carum carvi* seeds, and the other contains an extract of *C. carvi* (Nio/TQ and Nio/Carum, respectively). The resulting vesicles were characterized to assess their activity. Both thymoquinone (TQ) and noisome formulations containing *Carum carvi* showed controlled release compared to free TQ, allowing for a more controlled and sustained delivery of phytochemicals. The anticancer properties of these samples were analyzed by MTT assay, which showed that loaded liposomes had a higher anticancer effect on MCF-7 breast cancer cells compared to free TQ and *Carum carvi* extract alone. Flow cytometry studies further confirmed these results and provided additional information about the mechanism of action. The results of cell cycle analysis indicated that TQ, Nio/TQ and Nio/Carum formulations effectively inhibited cancer cell proliferation by inducing G2/M phase arrest, a key checkpoint for cell division. In addition, all three constructs (TQ, Nio/TQ, and Nio/Carum) inhibited MCF-7 cell migration, suggesting that they may also aid in the prevention of cancer. These results suggest that lipoids containing TQ and *Carum carvi* are novel and effective carriers for the encapsulation of poorly soluble phytochemicals. Their ability to improve solubility, control release, and enhance immunity makes them promising for breast cancer treatment. Liposome formulations that optimize the delivery of natural ingredients such as TQ and *Carum carvi* will provide cancer patients with new treatments that increase efficacy and reduce side effects.

Another study found that the drug was not Lawsone (2-hydroxy-1,4-naphthoquinone, also known as tannic acid, the main ingredient of the henna plant Lawsonia Spinosa) but a preparation containing ionic surfactants and cholesterol. In vitro, results showed that encapsulated Lawsone in liposomes

had increased anticancer activity against MCF-7 breast cancer cells compared to free Lawsone [33].

Figure 5: General Structure of Niosome



Plant-Based Bioactive: Nature's Anticancer Agents

There is a clear need for new antiviral drugs that are more effective and have fewer side effects. Plants are beneficial in creating these treatments. Scientific evidence supports the role of plants in preventing and treating cancer. 50-60% of approved vaccines are derived directly or indirectly from natural products. This study highlights some of the best plant-based foods with antioxidant properties. Both in vitro and in vivo studies have shown that they are anti-inflammatory. Plants derived from these compounds have potential as alternative therapies in preventing and treating cancer. Antibiotics are generally divided into four types: taxane diterpenes, vinca alkaloids, epipodophyllotoxins, and camptothecin derivatives. Other antibiotics such as combretastatin (a phenol), cephalosporins (an alkaloid), and ingenol mebutyrate may also be used in combination with plant bioactive compounds. Here is a brief discussion of some plant bioactive compounds used in cancer treatment. Many substances found in plants have been shown to have anti-inflammatory properties due to their biological activities.

Vinca Alkaloids

Catharanthus roseus alkaloids are a group of compounds derived from Periwinkle roseus (commonly known as the red periwinkle) of the family Apocynaceae. These alkaloids are two types of anti-inflammatory drugs commonly used to treat various types of cancer. Their cytotoxic effects are because the tubulin binding site is different from the taxane binding site. This disruption prevents microtubule polymerization and assembly, leading to metaphase arrest and ultimately cell death [34].

Vincristine was one of the first anticancer drugs approved by the FDA in 1963. Two natural alkaloids, vincristine and vinblastine, have been widely used in cancer treatment for nearly 50 years. Many synthetic drugs, such as vinorelbine and vindesine, have been developed and approved for medical use because of their effectiveness. These drugs are often used in conjunction with chemotherapy to treat many types of cancer, including leukemia, breast and lung cancer, Hodgkin's and non-Hodgkin's lymphoma, liver cancer, and Kaposi's sarcoma [35].

In recent years, many semisynthetic electronic products based on vinca alkaloids have been produced by labor-intensive and costly extraction. These derivatives, including vinorelbine, vincristine, vindesine, and vinflunine, are currently used in clinical practice. Vinblastine is reported to be obtained from fungi of the species Alternaria, while vincristine is produced by *Fusarium oxysporum*. In addition, *Fusarium solani* (a fungus isolated from the phloem of *Periwinkle L.*) produces a mixture of alkaloids [36].

Taxane Diterpenoids

Paclitaxel [Taxol] is widely considered one of the best-known plant-derived antibiotics. The cytotoxic properties of this taxane compound, a diterpene extracted from the bark of the Taxus brevifolia fruit (commonly known as the western yew), were first recorded by Wani and colleagues. In 1992, the U.S. Food and Drug Administration (FDA) approved paclitaxel for the treatment of ovarian cancer. Paclitaxel, the active ingredient in Taxol, is equally effective against a variety of cancers, including lung and stomach cancer. It is also used to treat many conditions, including head and neck cancer, endometrial cancer, breast cancer, prostate cancer, and other cancers. Paclitaxel binds to tubulin subunits, preventing their depolymerization, thereby stabilizing microtubules, disrupting mitosis, and finally inducing apoptosis [37].

Paclitaxel is a diterpene alkaloid with a complex chemical structure containing many chiral centers and rigid rings. Its structure has four fused rings, including a cyclodecane ring and an oxetane ring, making it particularly stable and biologically active. The structure and stereochemistry of the ring play an important role in the

ability of paclitaxel to interact with cellular components and exert its protective effects [54]. There is also a semi-synthetic derivative, docetaxel diterpene, which has made a name for itself in the treatment of various cancers, including breast, ovarian, pancreatic, prostate, and lung cancer. Many semi-synthetic drugs have been developed to increase cytotoxicity against cancer cells, reduce drug toxicity, and increase solubility. Taxanes exhibit anti-inflammatory effects by stabilizing microtubules, arresting the cell cycle, and preventing abnormal mitosis. Researchers found that paclitaxel also damages mitochondria and blocks the anti-apoptotic activity of B-cell leukemia protein 2 (Bcl-2) [55]. Cabazitaxel is a second-generation docetaxel derivative that has low toxicity and is cytotoxic to many docetaxel-resistant tumors. An important feature of cabazitaxel is its ability to cross the blood-brain barrier, something that other secans cannot achieve. Several paclitaxel analogs are currently under investigation, including larotaxel, octertaxel, miratаxel, and tilcetaxel [38].

A breakthrough came in 1993 when the endophytic bacterium Taxomyces andreaanae from the yew plant was discovered to produce small amounts of taxol. This discovery made it possible to grow paclitaxel from different species of endophytic bacteria, reducing production times and costs. The discovery of many endophytic bacteria capable of producing paclitaxel will also lead to the development of paclitaxel through microbial fermentation in the future [39].

Because all yew species have limited paclitaxel yield, scientists are looking for ways to increase their effectiveness. At the end of the 20th century, two independent research groups discovered two important paclitaxel precursors in the needles of the European yew (*Taxus baccata* L.): 10-desacetylbaccatin III and baccatin. Paclitaxel and its semi-synthetic water-soluble analog docetaxel (trade name Taxotere™) are currently produced in various semi-synthetic forms. However, further development is needed to meet future market demand for this important drug [40].

Podophyllotoxins

Podophyllotoxin is a product produced by *Podophyllum peltatum L.* and *Podophyllum emodi*Var (both from the Asteraceae family). The drug has been shown to inhibit cell growth by preventing tubulin polymerization, which disrupts mitotic spindle formation. Although podophyllotoxin binds reversibly to tubulin, its parent derivatives etoposide and teniposide act by inhibiting topoisomerase II, leading to DNA cleavage by topoisomerase II activity. Studies have also shown that podophyllotoxin can overcome multidrug resistance (MDR) in many types of cancer. These plants produce podophyllotoxin mainly in their roots and rhizomes, but podophyllotoxin has also been detected in stems, seeds, fruits, leaves, and wood parts and has been associated with endophytic bacteria. Among the podophyllotoxin-producing species, *Podophyllum hexandrum* Royle has a higher concentration of 4.3%. This advancement therefore opens the door to the virtual production of various podophyllotoxin derivatives to improve their therapeutic effects. These efforts require a comprehensive review of recent developments in podophyllotoxin research addressing other areas such as the consumption and utilization of natural podophyllotoxin products and bacterial growth [41].

Biotechnological methods have been developed to solve the problems associated with the development of podophyllotoxin. These difficulties include the ability of plants producing podophyllotoxin to die, the slowness and inconsistency of plants, the difficulty of producing synthetic products, and the generally low yield of natural products. Researchers are aiming to solve these problems and increase the efficiency of production processes using techniques such as genetic engineering, cell culture, and microbial manipulation. These innovations are important in meeting the demand for podophyllotoxin and its medicinal products [42].

The potential of fungal cells is more effective in somatic embryogenesis than other methods including tissue culture and macropropagation techniques. The main fungal species used for the commercial production of podophyllotoxins include * Fusarium oxysporum *, * Fusarium solani *, * Trametes pilosum *, * Alternaria spores *, * Mucor fragilis *, * Phialocephala fortinii * and * Aspergillus fumigatus *. These include *F [43].

Curcumin

Turmeric (*Curcuma longa*L.) is a perennial plant belonging to the Zingiberaceae family, native to Southeast Asia, and widely known for its use as a spice. Its rhizome contains curcumin, a plant polyphenol compound found in 2-5% of turmeric powder and frequently used in traditional Indian and Chinese medicine. In 1910, Lamp and

Milobedeska first determined the chemical structure of curcumin. It has a seven-carbon bond with two enone groups, an Î²-dicarbonyl unit, and two O-methoxyphenol aromatic rings. The IUPAC name of curcumin is (1E, 6E)-1, 7-bis(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione [64].

Due to its properties, many studies have been conducted on the antibacterial and anti-inflammatory properties of curcumin, including antibacterial, antifungal, antiviral, and anti-inflammatory diseases. Cancer. East Asians who eat turmeric as a staple food have a higher incidence of intestinal mucosal inflammation, leading to increased interest in the anti-inflammatory properties of curcumin. Curcumin acts as a chemosensitizer for certain chemotherapy drugs, such as gemcitabine, and works synergistically with other natural products, such as epigallocatechin-3-gallate, to defeat tumors and prevent recurrence. Recent studies have reviewed the literature on the anti-inflammatory effects of curcumin in animal models and human trials. Note that in cancer patients, curcumin MerivaÂ® (2,000 mg/day) in combination with gemcitabine improves the activity of the drug without causing serious side effects [44].

Curcumin exerts anticancer effects through several mechanisms, including reducing the number of cancer cells, inhibiting tumor growth, and promoting cancer cell apoptosis. Various methods of curcumin expression have been studied in vitro and in vivo in various cancer types, such as breast cancer and gastric cancer. For example, in HCT-116 and HT-29 cancer cells, curcumin increased apoptosis in response to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) by enhancing death receptor 5 (DR5) [66]. Many studies have reported the therapeutic effects of curcumin on various types of cancer, including blood, breast, head and neck, liver, prostate, ovarian, and colon skin cancer. This is due to curcumin's ability to modulate many signaling pathways and alter gene expression [45].

Homoharringtonine

Homoharringtonine is an ester derived from the alkaloid hahcetaxel, which occurs commonly in many plants of the *harringtonine* genus, such as *harringtonine* (Three Apogeonaceae). It has been used in China for over 50 years to treat patients with myeloid leukemia and is now approved for the treatment of myeloid leukemia. Homoharringtonine acts by inhibiting protein translation, competing with the ribosomal a site, and blocking the initial steps of protein synthesis. The semisynthetic form of homoharringtonine, omataxin methsuccinate, is effective in the treatment of myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML), particularly in response to azacitidine and dimethacin in patients resistant to hypomethylated drugs such as cytidine [46, 47].

Currently, homoharringtonine therapy combined with acrathromycin, daunorubicin, or cytarabine has achieved remission rates of up to 85% in acute myeloid leukemia (AML). Homoharringtonine has been shown to be an immunosuppressive agent that can protect against many leukemias despite resistance to drugs such as tyrosine kinase inhibitors. Recent studies have also shown that homoharringtonine can successfully eradicate all types of cancer, including those resistant to tyrosine kinase inhibitors [48, 49, 50].

CONCLUSION

In conclusion, this review demonstrates the potential of nanotechnology and herbal medicine to change cancer treatment. By combining the targeted delivery of lipid nanoparticles with the anti-inflammatory potential of botanical components, new therapeutic strategies can be developed. The combination of these two projects has the opportunity to overcome the limitations of cancer treatment, such as drug resistance and side effects. Delivery of products for lipid nanoparticles. Future research should focus on elucidating the mechanism of action of plant nanoparticles, evaluating their safety and efficacy in preclinical and clinical trials, and finding personalized treatment paths for patients. Through technological problems, and efforts in plants and medicine, scientists can develop better cancer treatment and self-healing, ultimately effectively benefiting patients and reducing the risk of major diseases worldwide.

This article discusses the importance of nanotechno logy in cancer treatment, particularly in the development of l ipid nanoparticles (LBNPs) that are more effective and provi de vaccines for diseases. The article highlights the advantag es of LBNPs, including their ability to improve tumor growt h, reduce side effects, and release drugs in response to specif ic stimuli. The article also discusses the use of nanotechnolo gy in cancer treatment, including the development of nanostr uctured lipid carriers (NLCs) and liposomes that can encaps ulate and deliver hydrophilic and hydrophobic drugs, increas

e drug solubility, and the development of pharmaceutical pro ducts. The article also discusses the potential of phytomedici ne and nanotechnology in cancer treatment, as well as the gl obal burden of cancer and the need for better treatment and prevention. The challenges in developing drug delivery syst ems, including the need for better and less toxic therapies, ar e also discussed. Overall, this article provides an overview o f the role of nanotechnology in cancer treatment and highlig hts its potential benefits and challenges.

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